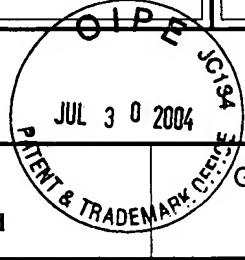
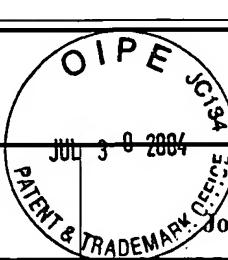


## TRANSMITTAL OF APPEAL BRIEF (Large Entity)

Docket No.  
2025.749

In Re Application Of: Wisniewski et al.

Serial No.  
10/056,237Filing Date  
January 25, 2002Examiner  
John K. FordGroup Art Unit  
3753Invention: FREEZING AND THAWING OF BIOPHARMACEUTICALS WITHIN A  
VESSEL HAVING A DUAL FLOW CONDUITTO THE COMMISSIONER FOR PATENTS:

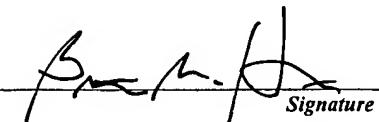
Transmitted herewith in triplicate is the Appeal Brief in this application, with respect to the Notice of Appeal filed on

The fee for filing this Appeal Brief is: \$330.00

A check in the amount of the fee is enclosed.

The Director has already been authorized to charge fees in this application to a Deposit Account.

The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 08-1935

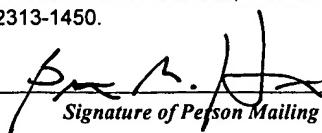


Signature

Dated: July 28, 2004

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I certify that this document and fee is being deposited on July 28, 2004 with the U.S. Postal Service as first class mail under 37 C.F.R. 1.8 and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.



Signature of Person Mailing Correspondence

Brett M. Hutton
<i>Typed or Printed Name of Person Mailing Correspondence</i>

CC:



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**Applicant:** Wisniewski et al.

**Group Art Unit:** 3753

**Serial No.:** 10/056,237

**Examiner:** John K. Ford

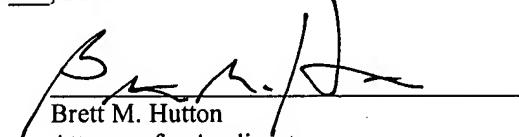
**Filed:** January 25, 2002

**Appeal No.:**

**Title:** FREEZING AND THAWING OF BIOPHARMACEUTICALS WITHIN A VESSEL HAVING A DUAL FLOW CONDUIT

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Mail Stop Appeal Brief-Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on July 28, 2004.



Brett M. Hutton  
Attorney for Applicant  
Reg. No. 46,787

Date of Signature: July 28, 2004

To: Mail Stop Appeal Brief-Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**Brief of Appellant**

Dear Sir:

This is an appeal from a final rejection, dated June 2, 2004, rejecting claims 1-8 and 27-42, a portion of the claims being considered in the above-identified application.

**Real Party In Interest**

This application is assigned to **Integrated Biosystems, Inc.** by virtue of an assignment executed on October 1, 1997 by the co-inventors and recorded with the United States Patent and Trademark Office on reel 9068, frame 0033. Therefore, the real party in interest is **Integrated Biosystems, Inc.**

**Related Appeals and Interferences**

To the knowledge of the appellant, appellant's undersigned legal representative, and the assignee, there are no other appeals or interferences which will directly affect or be directly affected by or having a bearing on the Board's decision in the instant appeal. There are, however, three other appeals that may be directly affected by or have a bearing on the Board's decision in the instant appeal. All of these appeals involve the same Examiner. These appeals involve the following applications.

- Serial Number 08/895,936, notice of appeal filed April 19, 2004, appeal brief filed June 10, 2004.
- Serial Number 09/881,909, notice of appeal filed April 19, 2004, appeal brief filed June 10, 2004.
- Serial Number 10/057,610, notice of appeal filed April 19, 2004, appeal brief filed June 10, 2004.

**Status of Claims**

This patent application was filed on January 25, 2002 as a continuation application of U.S. Application Serial No. 08/895,936, which is still pending before the U.S. Patent Office before the same Examiner, and which is also being appealed. As filed, the application included twenty-six (26) claims, of which three (3) were independent claims (i.e. claims 1, 9 and 25).

In an initial Office Action dated September 9, 2002, claims 1-26 were subject to restriction and election requirement. The Examiner considered the apparatus claims (i.e. claims 9-26) and the method claims (i.e. claims 1-8) as two distinct inventions. In appellant's response dated October 9, 2002, appellant elected to pursue the method claims, claims 1-8, and newly added method claims 27-42, which include three (3) independent claims, namely claims 1, 27 and 35. In appellant's response dated October 9, 2002; no claims were amended.

In a second Office Action dated April 10, 2003, claims 1-8 and 27-42 were rejected under 35 U.S.C. §112, second paragraph, because the Examiner considered the term "biopharmaceutical product" ambiguous. These same claims were also rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of the 1992 publication by Wisniewski and Wu and the 1986 Kalhori and Ramadhyani article entitled "Studies on heat transfer from a vertical cylinder with or without fins, embedded in a solid phase change medium" and U.S. Patent No. 2,114,642 to West. In appellant's response dated July 10, 2003, appellant traversed these rejection and no claims were amended. With this response, appellant provided the examiner with the second declaration of Mr. Wisniewski submitted in related application which addressed the request by the Examiner for more information concerning the Genentech device disclosed in the 1992 Wisniewski and Wu article.

Appellant received a third Office Action dated February 23, 2004 in which the Examiner sought additional information and clarification with respect to the second declaration of Mr. Winiewski. Despite the fact that the Examiner is the same examiner as in the other related applications and is fully aware of the first and second declarations of Mr. Wisniewski, appellant provided the Examiner with a copy of the first declaration of Mr. Wisniewski in its response dated March 3, 2004.

Appellant received a final Office Action dated June 2, 2004 repeating the 35 U.S.C. §112, second paragraph, and 35 U.S.C. §103(a) rejections of claims 1-8 and 27-42.

A Notice of Appeal to the Board of Patent Appeals and Interferences is filed herewith. The status of the claims is therefore as follows:

Claims allowed:	None
Claims objected to:	None
Claims rejected:	1-8 and 27-42
Claims canceled:	None
Claims withdrawn:	9-26

Appellant is appealing the rejection of claims 1-8 and 27-42.

#### Status of Amendments

Appellant proffered no response to the final Office Action dated June 2, 2004. The claims as set out in the Appendix include all prior entered amendments.

#### Summary of the Invention

Appellant's invention is directed to a method of preserving a biopharmaceutical product comprising placing a medium comprising a biopharmaceutical product into a vessel having an interior cavity defined by at least an interior wall of said vessel; actively cooling said interior wall using a fluid; actively cooling a heat exchange structure within said cavity by flowing a fluid through a dual flow conduit having one or more heat transfer members thermally coupled thereto; and freezing said medium within said vessel to preserve said biopharmaceutical product.

Issues

1. Whether the term "biopharmaceutical product" is ambiguous under 35 U.S.C. §112, second paragraph.
2. Whether claims 1-8 and 27-42 were rendered obvious under 35 U.S.C. §103(a) by the combined teachings of the 1992 publication by Wisniewski and Wu ("the 1992 Wisniewski and Wu publication") and the 1986 Kalhori and Ramadhyani article entitled "Studies on heat transfer from a vertical cylinder with or without fins, embedded in a solid phase change medium" ("1986 Kalhori and Ramadhyani article") and U.S. Patent No. 2,114,642 to West ("the '642 patent").
3. Whether appellant satisfied its duty under Rule 56.

Grouping of Claims

Appellant respectfully submits that the claims 1-8 and 27-42 are one separate group and claims 35-42 are a separate group.

Argument

**1. The Term "Biopharmaceutical Product" Is Not Ambiguous**

As noted, claims 1-8 and 27-42 stand rejected under 35 U.S.C. §112, second paragraph, because the Examiner considered the term "biopharmaceutical product" ambiguous. Reversal of this rejection is respectfully requested.

Appellant did not provide a definition in the specification for the term “biopharmaceutical product.” This term has a recognized meaning to those of ordinary skill in the art. The specification provided a number of examples of the type of biopharmaceutical products that may be processed by the present invention. The term “biopharmaceutical product” as set forth in the Specification in paragraph 29 includes, but is not limited to, proteins, cells, antibodies, medicines, plasma, blood, buffer solutions, viruses, serum, cell fragments, cellular components, and any other biopharmaceutical product.

Appellant also provided a definition of a “biopharmaceutical product” in a previous Amendment dated April 13, 2000 submitted in the parent Application Serial No. 08/895,936 as “a product derived from biological sources that has an intended therapeutic application and whose manufacturing is or will be regulated by pharmaceutical or veterinary regulatory agencies.” This definition is supported by the Declarations<sup>1</sup> of Chris J. Burman, V. Bryan Lawlis, Jr., and David A. Vetterlein (“the Declarants”), who are persons of ordinary skill in the art, which the Examiner is fully aware.

Despite support of the aforementioned understanding of the term of “biopharmaceutical products” from three persons of ordinary skill in the art having over 72 years of experience in the biotechnology and biopharmaceutical industry, the Office erroneously complicated the well-recognized understanding of this term. For example, the Office sets forth an opinion in concluding that orange juice and milk are biopharmaceutical products. In particular, the Examiner makes an unsupported statement in the final Office Action on page 22 that “[b]lood would probably freeze more in the manner of orange juice or milk given its nearly macroscopic cellular nature whereas virus in a suitable buffer solution or water would freeze in the manner of

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<sup>1</sup> The Examiner’s indication that these declarations are “not yet of record” is misplaced. Clearly, the Examiner was aware of these declarations and the definition for the term “biopharmaceutical products” from these persons of ordinary skill in the art because he was the Examiner of the parent Application Serial No. 08/895,936 and two other applications that rely upon these declarations. Moreover, the Examiner did not object to reference to and reliance on these declarations in appellant’s response dated July 3, 2003 or indicate that he did not have a copy of the same.

pure or salty water." (emphasis added). Based on such reasoning and unsupported statements, the Office indicates that the definition offered by the Declarants appears to be unworkable. (See page 14 of the Office Action). However, when not defined by an applicant in the specification, the words of a claim must be read as they would be interpreted by those of ordinary skill in the art, MPEP 2111.01, not by the Examiner himself.

In the final Office action, the Examiner also suggests that nothing in the declarations address why one designing freezing equipment for biopharmaceutical products disclosed in the specification would not look to the art of freezing water, orange juice or solids suspended in liquids. To the contrary, this issue has been addressed numerous times in previous responses and in the specification. As provided in the specification, appellant recognized, among other things, that the apparatus and method according to the aspects of the present invention are suited for use in processing biopharmaceutical products, as that term is understood by those of ordinary skill in the art. For example, the recited apparatus and method promotes uniform freezing at a rapid pace, which allows the biopharmaceutical product in the container to be frozen in as close to its native state as possible. (Specification, paragraph 32). Additionally, the present invention allows the freezing process to be done in a repeatable fashion so that a user can be assured that the freezing process is not causing batch to batch variations in the product. (Specification, paragraph 32).

Appellant respectfully submits that improper processing of biopharmaceutical product by, such as, for example, freezing and thawing, destroys biopharmaceutical products. In contrast, other products, such as, for example, orange juice, milk, water, particulate materials, and comestibles do not have the same processing concerns as biopharmaceutical products. Therefore, such products as orange juice, milk, water, particulate materials and comestibles, which do not require uniform freezing at a rapid pace which allow them to be frozen in as close to its native state as possible in order to prevent damage, are not included in the definition of

biopharmaceutical products. In particular, the method or apparatus used to process (e.g. freeze or thaw) these other products is not critical and will not destroy these other products.

Appellant, however, recognizes that, for example, a "buffer solution" can indeed be a biopharmaceutical product depending upon the contents of such a solution. In lab chemistry, buffers are associated with the maintaining of certain pH levels, while biopharma vocabulary (which is relevant to this application) uses the term buffers very broadly, including buffers with proteins (like Human Serum Albumin) or amino acids (multiple amino acids are used, for example, lysine or arginine) clearly having biomolecules which can be damaged by improper freezing. It is readily apparent that buffer solutions which are biologically based may indeed be regulated and be a biopharmaceutical product. Appellant respectfully submits that if, for example, a particular buffer solution is not derived from biological sources nor regulated by FDA, then it would not be considered a biopharmaceutical product under the aforementioned understanding of the term. The list of potential biopharmaceutical products provided in the specification sets forth examples of products which may be biopharmaceuticals. Because the term has a recognized meaning within the art, it is readily apparent to one of ordinary skill in the art what the term "biopharmaceutical product" means.

Therefore, Appellant respectfully traversed the opinions set forth by the Office in the Office Actions that orange juice, milk, water, comestibles, particulate materials and any other non-biopharmaceutical products (e.g. orange juice and milk) relied upon by the Office Action are considered a biopharmaceutical product and that vessels that freeze such materials are relevant to the delicate preservation of biopharmaceutical products. Appellants also requested the Office to support, by a reference or affidavit pursuant to M.P.E.P. § 2144.04, its position and opinion or in contradiction to the above definition and Declarations by three Declarants of ordinary skill in the art. (See Applicants' Response dated July 10, 2003, page 7). Specifically, appellant requested that the Office show that products such as orange juice, milk and

comestibles require uniform freezing at a rapid pace which allow them to be frozen in as close to its native state as possible in order to prevent damage. The Office ignored this request. Instead, the Examiner maintains his rejection and continues to rely on his own personal opinion and knowledge, without providing a supporting reference or affidavit.<sup>2</sup> (See pages 17-22 of the final Office Action).

Appellant respectfully submits that one of ordinary skill in the art is capable of distinguishing and classifying which products are and are not biopharmaceutical products based on the above definition, as evidenced by, for example, the Declarants classification of milk and orange juice as not being pharmaceutical products in their Declarations. For example, one of ordinary skill in the art is capable of determining which proteins, cells, antibodies, medicines, plasma, blood, buffer solutions, viruses, serum, cell fragments, cellular components, and any other biopharmaceutical product are considered a biopharmaceutical product under the above definition.

Finally, the reliance by the Office in the final Office Action (page 21) on an interpretation of a “would-be infringer” in rejecting the term “biopharmaceutical products” is improper. Under M.P.E.P. § 2173.02, definiteness of claim language must be analyzed in light of the content of the particular application disclosure, the teachings of the prior art and the claim interpretation that would be given *by one possessing the ordinary level of skill in the pertinent art at the time the invention was made*. Appellant respectfully submits that the proper inquire is how “biopharmaceutical products” will be interpreted by a person of ordinary skill in the art,

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<sup>2</sup> The Examiner's only response in support of his “understanding” is that “counsel says nothing to contradict the Examiner's understanding.” However, an applicant is not required to contest the Examiner's understanding when specifically requesting support for such understanding in an affidavit or other form. The Examiner refused to provide such proof. The Examiner cannot simply reply to an applicant's request for support of the Examiner's alleged (an unsupported) understanding by arguing that applicant's counsel did not say anything about it, when applicant's counsel initially requested supporting proof from the Examiner.

not by a “would be” infringer. Therefore, the Office, in maintaining the rejection of the term “biopharmaceutical products” on this basis, failed to follow this approach.

Accordingly, Appellant respectfully submits that the term “biopharmaceutical product” is definite.

**2. Claims 1-8 And 27-42 Are Patentable Over The Combined Teachings Of The 1992 Wisniewski And Wu Publication, The 1986 Kalhori And Ramadhyani Article And The ‘642 Patent**

As noted, claims 1-8 and 27-42 stand rejected under 35 U.S.C. §103(a) as obvious over the combined teaching of the 1992 Wisniewski and Wu Publication, the 1986 Kalhori and Ramadhyani article and the ‘642 patent.

In support of this rejection, the Office relies on features in the cited prior art that are not recited in the claims. For example, the Office makes reference to a “thermal transfer bridge” and “bottom up freezing”, which are not specifically recited in the claims of the instant application.

Further, the Examiner’s statement that counsel concedes the validity of the “Examiner’s legitimate motivational statements” to combine the 1986 Kalhori and Ramadhyani article and the 1992 Wisniewski and Wu publication is simply incorrect. Appellant never conceded such a statement. In fact, the Office completely ignores the arguments set forth by appellant in the response dated July 10, 2003 in which it describes the disclosure of the references cited by the Examiner and specifically states that there is no motivation or suggestion to combine these references along with a detailed explanation why such a combination is improper. (See pages 10-12 of Appellant’s July 10, 2003 Response). In fact, as discussed in more detail below, the Examiner admits the difficulty of determining temperature distributions for different types of

vessels that process different materials, which makes combination of such vessels or parts thereof unpredictable and, thus, non-obvious based on his own admissions.

**a. The Office Improperly Combined The Cited References**

Initially, appellant notes that each of the references relied upon by the Office to reject the claims teach completely different processes to freeze products by using completely different principles. In fact, the cited references teach away from each other and, therefore, there is no motivation or suggestion to combine. Further, aside from the 1992 Wisniewski and Wu publication, none of the cited references disclose biopharmaceutical products or recognize the problems associated with processing such products.

**i. The 1992 Wisniewski and Wu Publication**

Specifically, the 1992 Wisniewski and Wu publication discloses a device having an internal heat transfer coil pipe with fins welded to the external surface of the coil pipe. The fins attached to the coil are very small and thin and were designed only to aid the freezing around the loop coil in order to increase the relatively small surface area of the loop pipe (e.g. adding more cold surface area). The outside of this device is cooled. A copy of this device is reproduced, for convenience, below:

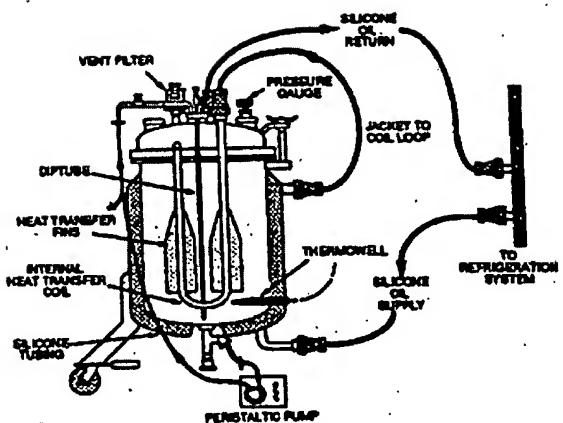


Figure 1. Freeze-thaw Vessel: Thawing Configuration

As shown, the fins attached to the pipe coil are very small and thin and were designed only to aid the freezing around the loop coil in order to increase the relatively small surface area of the loop pipe (e.g. adding more cold surface area). (Second Wisniewski Declaration, ¶8). The device disclosed in this publication does not have a dual-flow conduit, as recited in the claims.

## ii      The 1986 Kalhori and Ramadyani Article

The 1986 Kalhori and Ramadyani article involves the investigation of the solidification of a paraffin<sup>3</sup> in a smooth, thin-walled metal cylindrical tank having an electrical strip heater wrapped around the upper part of the tank. The purpose of the investigation was to demonstrate that natural convection in the liquid phase plays a dominant role in melting and to a certain extent influences solidification. The investigation involves a comparison of the temperature distributions in the paraffin using a plain vertical cylinder in the tank and a vertical cylinder with fins, during cyclic melting and freezing. This cyclic cooling and heating generates convectional currents in the liquid phase of the medium. There is no disclosure or suggestion that the external tank walls are actively cooled. In contrast, the vessel is wrapped with an

<sup>3</sup> Paraffin is a white, waxy, odorless, tasteless solid substance consisting of a mixture of straight chain saturated hydrocarbon used to make, for example, candles, sealing preserving jars, waterproofing paper

electrical ban heater to warm the medium from the outside while the cylinder within is cooling it. Therefore, the temperature closer to the external wall from within the vessel increases, the temperature closer to the cylinder decreases, and heat transfer to the paraffin occurs from the cylinder.

The 1986 Kalhori and Ramadyani article simply concludes that the use of fins works better than no fins. However, this fact was already recognized in the 1992 Wisniewski and Wu publication as shown by the disclosure of the coil pipe having fins attached thereto. There is absolutely no disclosure or suggestion in the 1986 Kalhori and Ramadyani article of biopharmaceutical product or a discussion or recognition of the problems associated with processing biopharmaceutical product. Therefore, there is no motivation or suggestion to combine the 1986 Kalhori and Ramadyani article with the 1992 Wisniewski and Wu article because the 1986 Kalhori and Ramadyani article does not involve, or recognize the problems associate with processing, biopharmaceutical products.

There is also no motivation to combine the interior structure disclosed in the 1986 Kalhori and Ramadyani article with the container disclosed in the 1992 Wisniewski and Wu publication because the devices disclosed in both articles involve different principles of freezing. Specifically, the device disclosed in the 1992 Wisniewski and Wu article cools the container from the outside and the inside and the 1986 Kalhori and Ramadyani article heats the container on the outside while cooling the container inside. Therefore, contrary to the Examiner's suggestion, it would not be obvious to simply put the interior structure disclosed in the 1986 Kalhori and Ramadyani article in the tank disclosed in the 1992 Wisniewski and Wu publication because one of ordinary skill in the art would not be motivated to look towards the 1986 Kalhori and Ramadyani article to combine with the 1992 Wisniewski and Wu publication due to problems associated with processing biopharmaceutical products and the fact that the

device in the 1992 Wisniewski and Wu article already uses fins and cools the device from the inside using the coil pipe.

In support of this combination, the Office simply concludes that it would be obvious to one of ordinary skill in the art to replace the heat exchanger and fins of the 1992 Wisniewski and Wu publication with the heat exchanger and fins shown in the 1986 Kalhori and Ramadhyani article to improve heat transfer and to facilitate ease of construction as well as to facilitate easy removal from the frozen mass. However, the Office fails to explain how substituting one structure for another in a vessel using completely different principles would produce the same desirable freezing results of biopharmaceutical products, especially in view of the Examiner's own statements on page 8 in the final Office Action dated June 2, 2004 that:

Moreover this Examiner who holds a masters degree in Engineering from Princeton University, does not believe that there is anyone who can model or calculate these temperature profiles without the aid of sophisticated computers and/or experimental work.

and on page 11 in the same Office action that:

[T]he temperature distribution must either be measured or generated by very sophisticated computer programs.

### **iii. The '642 Patent**

The '642 patent is directed to the acceleration of the production of frozen articles such as milk, sherbet and similar substances, not to the preservation of biopharmaceutical products. The '642 patent describes freezing that prevents sugar deposition form the original solution. The object of this patent is not to optimize the preservation of biopharmaceutical products by freezing, but rather to fast freeze to make milk and sherbet look a certain way (e.g appealing to consumers). In the '642 patent, liquid refrigerant gets to the header (3) where it boils in cup

(15) onto which the container with product (8) is slipped. Since the refrigerant boils inside the cups (15), then there is no control of freezing (e.g. very fast freezing, see page 2, lines 60-66). Contrary to the Office's statements, the '642 patent does not show any dual flow conduit.

**iv. No Motivation To Combine**

Therefore, the 1992 Wisniewski and Wu publication, the 1986 Kalhori and Ramadyani article and the '642 West patent each freeze products by completely different ways using completely different freezing principles. As such, these references teach away from each other and there is simply no motivation to combine the same. Specifically, the 1986 Kalhori and Ramadyani article teaches heating the medium from the outside of the cylinder while the structure within was cooling it. In sharp contrast, the 1992 Wisniewski and Wu publication teaches cooling the outside and inside of the cylinder. Finally, the '642 West patent discloses a method of freezing completely different from the device in the 1992 Wisniewski and Wu publication and the 1986 Kalhori and Ramadyani article. Appellant respectfully submits that one of ordinary skill in the art would not look towards a device that is heated on the outside to combine with a device that was cooled on the inside because the methods and principles of freezing used in both devices are completely different. This conclusion is reinforced by statements made by this same Examiner in the final Office Action of the parent application (Serial No. 08/895,936) highlighting the difficulty in determining the temperature distribution of these types of devices. These statements include the following:

The Examiner . . . does not believe that there is anyone who can model or calculate these temperature profiles without the aid of sophisticated computers and/or experimental work. . . . The processes of modeling natural convection and moving-front phase change occurring together with sub-cooling is, to the Examiner's knowledge, is state of the art or beyond the state of the art in numerical solutions on computers. See Final Office Action in Serial No. 08/895,936, page 8.

It is respectfully submitted that these freezing phenomena are so complex that no human being including one with nearly 30 years of experience can accurately predict such results. Purporting to have such ability only diminishes ones credibility. See Final Office Action in Serial No. 08/895,936, page 10.

Thus, researchers, other than Mr. Wisniewski, state that accurate modeling of phase change heat transfer in tanks with finned element such as shown in Figure 3 of the K&R article can only be done by computers or by direct empirical measurement. See Final Office Action in Serial No. 08/895,936, page 11.

[T]he temperature distribution must either be measured or generated by very sophisticated computer programs, which have had their validity checked against measured data. See Final Office Action in Serial No. 08/895,936, page 12.

Mr. Wisniewski's guesswork even in declarative form is simply no substitute for real evidence. Neither he nor any other person on the planet is in a position to properly guess at the actual temperature distribution. See Final Office Action in Serial No. 08/895,936, page 14.

Accordingly, the Office admits that even those of ordinary skill in the art cannot look at and simply combine the cited references and arrive at the desired result disclosed in the Specification and recited in the claims of the present invention without experimentation or the aid of a computer. This is also in total contradiction to the Examiner unsupported conclusion that "motivation of placing the dual flow conduit of the Kalhori and Ramadhyani in the 1992 Wisniewski and Wu device in place of the heat exchange structure shown there" on page 24 of the final Office Action. The Examiner cannot, on one hand, argue that "no human being" can predict the temperature profiles of these vessels and, on the other hand, simply conclude that substituting one structure for another will provide the desired results, e.g., improved heat transfer or facilitate anything. By the Examiner's own admissions, such a substitution is not obvious and is unpredictable to any human being, especially, as appellant pointed out in its July 10, 2003 response, since these two references disclose completely different methods of processing two completely different types of materials. Specifically, the 1992 Wisniewski and Wu article discloses the processing of biopharmaceutical products by cooling the outside while

the 1986 Kalhori and Ramadyani articles discusses the processing of paraffin by heating the outside of the vessel. Therefore, there is simply no suggestion or motivation to combine the structure within the 1986 Kalhori and Ramadyani article with the cooled cylinder of the Genentech device.

The Examiner's statement on page 24 that counsel has not traversed the Examiner's alleged motivational statements is simply not true. The Examiner in the final Office Action completely ignores appellant's argument set forth in its response dated July 10, 2003, concerning the different methods of freezing products disclosed in these cited references using completely different principles. Since the Office Action failed to address these arguments, appellant respectfully submits that this deficiency at least renders incomplete a rejection based on an alleged combination of the cited references. For at least this reason, reversal of the obviousness rejection and allowance of the claims are respectfully requested.

**b. The Cited References Do Not Disclose The Recited Method**

Appellant's independent claims specifically recite: "flowing a fluid through a dual flow conduit having one or more heat transfer members thermally coupled thereto." Appellant's independent claims also require active cooling of the interior wall of the vessel.

As admitted by the Office, the 1992 Wisniewski and Wu publication fails to teach or suggest appellants' claimed element of a dual flow conduit. The 1986 Kalhori and Ramadyani article fails to disclose active cooling of the exterior wall of the vessel. In contrast, the device in this article heats the exterior wall. Finally, as explained above, the '642 patent describes a completely different apparatus and method for freezing non-biopharmaceutical products.

Therefore, in view of the reasons provided above, the 1992 Wisniewski and Wu publication, the 1986 Kalhori and Ramadyani article, and the '642 patent fails to disclose each

and every limitation recited in the claims and there is no motivation or suggestion to combine these references.

### **3. Appellant Satisfied Their Duty Under Rule 56**

In the second Office Action dated April 10, 2003, the Examiner requested additional information concerning the prior art devices disclosed in the specification and the Genentech device disclosed in the 1992 disclosure of Wisniewski and Wu. The Examiner also suggested that the inventors contact Genentech to obtain the dimensions of the prior art Genentech device. However, the Examiner incorrectly assumed that the appellants were in possession of this information because they worked on the Genentech device more than a decade ago.

In appellant's response dated July 10, 2003, appellant made clear to the Examiner that the applicants do not work for Genentech and were not in possession of the 1992 Genentech device. In an effort to further assist the Office, one of the inventors, Mr. Wisniewski, submitted a Second Declaration that provided as much information that he could remember concerning the Genentech device.

In a third Office Action dated February 23, 2003, the Examiner considered appellant's response dated July 10, 2003 as not fully responsive to the second Office Action because the declaration of Mr. Wisniewski referred to the wrong serial number. However, the Examiner completely ignored appellant's statement in the July 10, 2003 response that noted the different serial number but explained that the declaration was submitted for the same request. The Examiner also suggested that applicants submit a third declaration to explain why they did not contact Genentech.

Appellant promptly filed a response on March 3, 2000 by submitting a copy of the first declaration and Mr. Wisniewski and again explaining that these declarations are directed to the

same questions and that they have disclosed as much information as they can remember concerning the prior art, especially the Genentech device. Therefore, appellant has satisfied their duty under Rule 56 and the Office should have considered appellant's response to the second Office Action as a complete reply under 37 C.F.R. §1.105(a)(3).

In the final Office Action, the Examiner provides his personal response to each paragraph in the declarations submitted by Mr. Wisniewski. However, these declarations were not submitted to support the claims in the present application, but rather to contest the Examiner's accusations that appellant failed to provide information concerning the prior art, specifically the Genentech device disclosed in the 1992 Wisniewski and Wu article. A response to the Examiner's position concerning the substance of these declarations is not necessary at this point in time because, as mentioned above, the claims in the present application do not recite a "thermal bridge" or a relationship (in distance) between the fins and interior wall of the vessel.

Appellant provided the Office with as much information concerning the prior art that is presently known or readily available. Whether or not Genentech is a competitor or customer (both are actually true), Rule 56 does not require an applicant to contact another company for a competitive device in order to conduct experiments using its own equipment to perform testing to support the Examiner's unsupported beliefs and speculation, which have no bearing upon the claims. Clearly, this request exceeds the requirement under Rule 56.

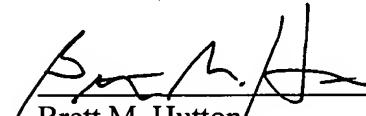
Therefore, appellant submits that all information that is known and readily available was submitted.

**Conclusion**

For the reasons set forth above, reversal of the rejections and allowance of this application are respectfully requested.

Dated: July 28, 2004

Respectfully submitted,



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## APPENDIX

### CLAIMS FOR APPLICATION SERIAL NUMBER 10/056,237

1. A method of preserving a biopharmaceutical product comprising:
  - placing a medium comprising a biopharmaceutical product into a vessel having an interior cavity defined by at least an interior wall of said vessel;
  - actively cooling said interior wall using a fluid;
  - actively cooling a heat exchange structure within said cavity by flowing a fluid through a dual flow conduit having one or more heat transfer members thermally coupled thereto;
  - freezing said medium within said vessel to preserve said biopharmaceutical product.
2. The method of claim 1, wherein said dual flow conduit comprises a core member defining an interior passage adapted to receive a fluid and an outer member spaced from the core member and defining an outer passage with the core member, wherein the inner and outer passages are in fluid communication with each other to define a flow path for a fluid.

3. The method of claim 2, further comprising directing fluid down the interior passage and up the outer passage.
4. The method of claim 1, wherein said dual flow conduit is centrally located within said interior cavity.
5. The method of claim 1, wherein said structure is removably mounted within said interior cavity of said vessel.
6. The method of claim 1, wherein said one or more heat transfer members are fins.
7. The method of claim 6, wherein said fins extend radially outward from said dual flow conduit.

8. The method of claim 7, wherein said fins are configured symmetrically around said dual flow conduit to form substantially similar compartments within said interior cavity.

9. An apparatus for preserving a biopharmaceutical product comprising:

a vessel adapted to receive a medium comprising a biopharmaceutical product, said vessel having an interior cavity defined by, at least, an interior wall of said vessel, said interior wall adapted to be actively cooled using a fluid;

a heat exchange structure being positioned within said cavity having one or more heat transfer members thermally coupled thereto, said heat exchange structure comprising a dual flow conduit adapted to be actively cooled using a fluid.

10. The apparatus of claim 10, wherein said dual flow conduit comprises a core member defining an interior passage adapted to receive a fluid and an outer member spaced from the core member and defining an outer passage with the core member, wherein the inner and outer passages are in fluid communication with each other to define a flow path for a fluid.

11. The apparatus of claim 10, wherein fluid is directed down the interior passage and up the outer passage.
12. The apparatus of claim 10, wherein said core member and said outer member are tubular.
13. The apparatus of claim 9, wherein said heat exchange structure is removably mounted within said cavity.
14. The apparatus of claim 9, wherein said one or more of said heat transfer members are fins.
15. The apparatus of claim 14, wherein said fins are configured to form freezing compartments in said interior cavity.

16. The apparatus of claim 10, wherein said outer member comprises an end piece adapted to receive fluid flowing through the interior passage defined by said core member.

17. The apparatus of claim 16, wherein said end piece includes a heat exchange member.

18. The apparatus of claim 17, wherein said heat exchange member of said end piece extends towards said interior wall.

19. The apparatus of claim 9, wherein said one or more of said heat transfer members extend radially from said heat exchange structure.

20. The apparatus of claim 9, wherein said dual flow conduct is positioned in the center of said vessel.

21. The apparatus of claim 9, wherein said heat exchange structure includes a plurality of heat transfer members configured to form freezing compartments within said interior cavity.

22. The apparatus of claim 9, wherein said interior wall includes one or more heat transfer members extending towards said structure.

23. The apparatus of claim 22, wherein said one or more heat transfer members extending from said interior wall extend towards said one or more heat transfer members of said heat exchange structure.

24. The apparatus of claim 9, wherein said dual flow conduit promotes bottom to top freezing.

25. An apparatus for processing a biopharmaceutical product comprising:  
a vessel adapted to receive a medium comprising a biopharmaceutical product,  
said vessel having an interior wall defining an interior cavity, said interior wall adapted to be  
actively cooled using a fluid;  
a plurality of heat exchange structures within said interior cavity, at least one of  
said plurality of heat exchange structures comprising a dual flow conduit adapted to be actively  
cooled using a fluid, wherein at least one of said plurality of heat exchange structures comprises  
one or more heat transfer members.

26. The apparatus of claim 25, wherein said dual flow conduit comprises a core  
member defining an interior passage adapted to receive a fluid and an outer member spaced from  
the core member and defining an outer passage with the core member, wherein the inner and  
outer passages are in fluid communication with each other to define a flow path for a fluid.

27. A method for facilitating the processing of a biopharmaceutical product  
comprising:  
providing a vessel adapted to receive a medium comprising a biopharmaceutical  
product therein, said vessel having an interior cavity defined by at least an interior wall of  
said vessel;  
providing a passage for actively cooling said interior wall using a cooling fluid;  
and

providing a heat exchange structure within said cavity, said heat exchange structure including a dual flow conduit having one or more heat transfer members thermally coupled thereto, said dual flow conduit defining a passage for actively cooling the one or more heat exchange members using a cooling fluid.

28. The method of claim 27, wherein said dual flow conduit comprises a core member defining an interior passage adapted to receive a fluid and an outer member spaced from the core member and defining an outer passage with the core member, wherein the inner and outer passages are in fluid communication with each other to define a flow path for a fluid.

29. The method of claim 28, further comprising providing fluid to direct down the interior passage and up the outer passage.

30. The method of claim 27, wherein said dual flow conduit is centrally located within said interior cavity.

31. The method of claim 27, wherein said structure is removably mounted within said interior cavity of said vessel.

32. The method of claim 27, wherein said one or more heat transfer members are fins.
33. The method of claim 32, wherein said fins extend radially outward from said dual flow conduit.
34. The method of claim 33, wherein said fins are configured symmetrically around said dual flow conduit to form substantially similar compartments within said interior cavity.
35. A method of processing a biopharmaceutical product comprising:  
providing a vessel adapted to receive a medium comprising a biopharmaceutical product therein, said vessel having an interior cavity defined by an interior wall of said vessel and a heat exchange structure within said cavity, said heat exchange structure having a dual flow conduit having one or more heat transfer members thermally coupled thereto;  
placing a medium comprising a biopharmaceutical product within said vessel;

actively cooling said interior wall using a cooling fluid;  
actively cooling said heat exchange structure by flowing a fluid through  
the dual flow conduit; and  
freezing the medium within said vessel to preserve said biopharmaceutical  
product.

36. The method of claim 35, wherein said dual flow conduit comprises a core member defining an interior passage adapted to receive a fluid and an outer member spaced from the core member and defining an outer passage with the core member, wherein the inner and outer passages are in fluid communication with each other to define a flow path for a fluid.

37. The method of claim 36, further comprising directing fluid down the interior passage and up the outer passage.

38. The method of claim 35, wherein said dual flow conduit is centrally located within said interior cavity.

39. The method of claim 35, wherein said structure is removably mounted within said interior cavity of said vessel.

40. The method of claim 35, wherein said one or more heat transfer members are fins.

41. The method of claim 40, wherein said fins extend radially outward from said dual flow conduit.

42. The method of claim 41, wherein said fins are configured symmetrically around said dual flow conduit to form substantially similar compartments within said interior cavity.